

1103326-0630

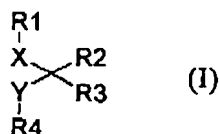
RECEIVED
CENTRAL FAX CENTER

JUL 06 2007

In the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (currently amended) A compound of general Formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R₁ is selected from the group consisting of:

C₂-C₆ C₁-C₆ alkyl, substituted with one or more basic groups selected from amino, amidino and guanidino; ~~and~~

six-membered aromatic heterocyclyl containing a single heteroatom, which heteroatom is nitrogen, and substituted with one or more basic groups selected from amino, amidino and guanidino; ~~and~~

six-membered aliphatic heterocyclyl containing a single heteroatom, which heteroatom is nitrogen;

R₂ is selected from the group consisting of H, methyl, halogen, and hydroxy;

R₃ is selected from the group consisting of COOR₅, SO(OR₅), SO₃R₅, P=O(OR₅)₂, B(OR₅)₂, P=OR₅(OR₅), and tetrazole; ~~and a carboxylic acid isostere;~~

R₄ represents a $\begin{array}{c} O-R_5 \\ | \\ -P- \\ || \\ O \end{array} R_6$ -group;

1103326-0630

R₅ is H, C₁-C₆ alkyl, or aryl;

R₆ is C₁-C₆ alkyl, aryl, cycloalkyl, or an optionally N-substituted

H₂N-CH(Z)-CONH-CH(Z)- or H₂N-CH(Z)- group;

X is C(Z)₂;

Y is selected from the group consisting of O and S; and

Z is independently selected from the group consisting of H, C₁-C₆ alkyl, aryl, and cycloalkyl.

2. (currently amended) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R₁ is selected from the group consisting of:

six-membered aromatic heterocyclyl containing a single heteroatom, which heteroatom is nitrogen, and substituted with one or more basic groups selected from amino, amidino and guanidino; and

six-membered aliphatic heterocyclyl containing a single heteroatom, which heteroatom is nitrogen;

R₃ is COOR₅;

Y is O; and

Z is independently H or C₁-C₆ alkyl.

3-26. (cancelled)

27. (previously presented) The compound according to claim 1 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

1103326-0630

wherein:

R₆ is optionally substituted by one or more selected from the group consisting of acyl, acylamino, C₁-C₆ alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, hydroxy, oxo, nitro, thio, Z₂N-CO-O-, ZO-CO-NZ- and Z₂N-CO-NZ-;

in which said C₁-C₆ alkyl, cycloalkyl, and aryl are each optionally substituted by one or more selected from the group consisting of acyl, acylamino, C₁-C₆ alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, hydroxy, oxo, nitro, thio, Z₂N-CO-O-, ZO-CO-NZ- and Z₂N-CO-NZ-; and

each Z, which is defined in claim 1, is independently and optionally substituted by one or more selected from the group consisting of acyl, acylamino, C₁-C₆ alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl, aroylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, hydroxy, oxo, nitro, thio, Z₂N-CO-O-, ZO-CO-NZ- and Z₂N-CO-NZ-.

1103326-0630

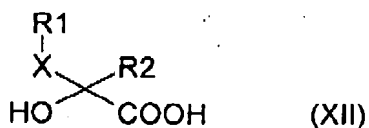
28. (previously presented) The compound according to claim 27 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

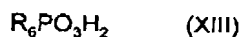
R₆ is optionally substituted by one or more selected from the group consisting of C₁-C₆ alkyl, aryl and ZO-CO-NZ-,

in which said C₁-C₆ alkyl and aryl are each optionally substituted by one or more selected from the group consisting of aryl, oxo and ZO-CO-NZ-, and each Z, which is defined in claim 1, is independently and optionally substituted by aryl.

29. (previously presented) A process for the preparation of a compound according to any one of claims 1, 2, 27 and 28, wherein R₁, R₂, R₄, R₅, R₆, X and Z are as defined in claim 1, R₃ is COOR₅, and Y is O, comprising the step of:
reacting a compound of Formula XII,



wherein X, R₁ and R₂ are as defined in claim 1, with a compound of Formula XIII,



1103326-0630

wherein R₆ is as defined in claim 1, in the presence of a coupling reagent under standard conditions.

30. (previously presented) A pharmaceutical formulation comprising a therapeutically effective amount of a compound according to any one of claims 1, 2, 27 and 28 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

31. (withdrawn) A method for inhibiting carboxypeptidase U, comprising administering an effective amount of a compound according to any one of claims 1, 2, 27 and 28.

32. (currently amended) A pharmaceutical formulation comprising:
(i) a compound of Formula I as defined in any one of claims 1, 2, 27 and 28, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; and
(ii) one or more antithrombotic agents with a different mechanism of action from that of component (i),
in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

33. (withdrawn) A method both for inhibiting carboxypeptidase U and for achieving an antithrombotic effect via a different mechanism, which method comprises administering a therapeutically effective total amount of:
(i) a compound as defined in any one of claims 1, 2, 27 and 28, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and

(ii) one or more antithrombotic agents with a different mechanism of action from that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

34. (withdrawn) A method both for inhibiting carboxypeptidase U and for achieving an antithrombotic effect via a different mechanism, which method comprises administering the formulation according to claim 32.

35. (canceled)

36. (withdrawn) The process according to claim 29, wherein the coupling reagent is selected from the group consisting of:
(i) dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP);
(ii) (benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBop)/ diisopropylethylamine (DIPEA);
and
(iii) SOCl_2 .

37. (withdrawn) The formulation according to claim 32, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P_2T) antagonist.

38. (withdrawn) The method according to claim 33, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P_2T) antagonist.

39. (withdrawn) A method for treatment of thrombosis and hypercoagulability, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1, 2, 27 and 28.